REMARKS

The Official Action of December 9, 2004, and the prior art relied upon therein have been carefully studied. The claims in the application are now claims 1-9, 11 and 13-27, and these claims define patentable subject matter, not only for the reasons previously submitted, but for the additional reasons elaborated upon below. Accordingly, applicants again respectfully request favorable reconsideration and allowance.

Undersigned on behalf of applicants thank the examiner for the courtesies provided during the short telephone conference on May 6, 2005, between undersigned and Examiner Pratt. At that time, applicants pointed out that the Office Action Summary indicates that the Action is "non-final" whereas the end of the Office Action indicates that it is final. Examiner Pratt graciously agreed to treat the last Office Action as non-final. Accordingly, there should be no question as to entry of the amendments presented above.

A number of amendments have been made in the specification for improved clarity. For example, in the paragraph originally spanning pages 5 and 6 of the specification, the term "solution" in many places has been

changed to "mixture", as the word "solution" was used in the broad sense rather than the technical sense. These amendments are consistent with amendments made in paragraph (i) of claim 1, already previously appearing in claim 25. Clear support is found in the bottom paragraph on page 6 of applicants' specification. That the particle size reduction of the lipophilic compound in step (i) be carried out in the presence of water or a water miscible solvent (or mixture thereof) rather than in an organic solvent (as is the case with the primary Sato patent) is an important feature of the present invention, as is pointed out in the attached Declaration of Dr. Blatt.

Support for the amendment in step (i) has been explained above. Support for the amendment of step (vi) is to be found on page 9, lines 7 and 8 of applicants' specification, and part of the added subject matter previously appeared in original claim 10.

Support for the amendment adding the concentration of the acidic solution in step (v) is found at page 6, line 6 of applicants' specification.

Claims 10 and 12 have been canceled, as subject matter of such claims has now been incorporated into claim 1.

New claims 26 and 27 have been added. Claim 26 finds support in applicants' specification at page 6, lines 9 and 10. Claim 27 finds support in applicants' specification at page 5, lines 26 and 30. These claims are patentable because they depend from and incorporate the subject matter of patentable claim 1.

Claims 1-4, 6, 8-11, 13,1 4 and 20-22 have been rejected as obvious from Sato in view of Silbiger, Kantor and Patel. Claim 12 has been similarly rejected as obvious under §103 from the same combination of references, further in view of Francois. These rejections are respectfully traversed.

As the subject matter of claim 12 has been incorporated into claim 1, applicants understand that the rejection of claims 1-4, 6, 8, 9, 11-14, 20 and 22 would presumably be based on the five-reference combination of Sato in view Silbiger, Kantor, Patel and Francois. Applicants believe and again respectfully submit that applicants' invention would not have been obvious from the proposed combination for the reasons set forth in the preceding Reply. However, applicants now wish to go forward with emphasis on primarily two points in which Sato is deficient and there is no known subsidiary reference which would lead the person of ordinary skill in the art to modify

Sato so that the resultantly modified Sato would correspond to or even approach applicants' claimed invention.

The first of these points involves the avoidance of an organic solvent in step (i) of the present invention. The reason for this, as explained in Dr. Blatt's attached Declaration, is because organic solvent increases the complexity of the processing, adds unnecessary costs, and the presence of the organic solvent can undesirably increase the volume of the material to be encapsulated, thus inherently and unavoidably increasing the size of the microcapsules per unit dose of each microcapsule, all of which are contrary to and/or undesirable to the present invention. On the contrary, Sato **requires** an organic solvent at this stage, due to the subsequent utilization of phase inversion to form the microcapsules.

Please especially note steps (4),(5)and (6)(a) of the Sato process at column 1, lines 35-49, which requires the presence of solvent. Also please see the paragraph spanning columns 4 and 5 of Sato where the organic solvents required by Sato are further explained.

The rejection relies of Silbiger for the concept of forming beadlets by dropping a sodium alginate solution into a calcium containing solution, but there are at least two reasons why it would not have been obvious to modify

Sato by adopting the bead forming procedure of Silbiger and discarding Sato's phase inversion method. First in this regard, the phase inversion method of Sato is mandatory, and requires the presence the organic solvent as pointed out above. To modify Sato by adopting Silbiger's bead forming procedure would be to fly in the face of Sato, and that would be the antithesis of obviousness.

Second, the system of Silbiger is more than simply forming beads by dropping an alginate solution into a calcium chloride solution. Thus, the Silbiger system comprises an injector having three coaxial tubular members 11, 12 and 13. A cell suspension is fed through the central opening 14, an alginate solution coaxially thereabout through an annular opening 15, and gas thereabout through a second annular opening 16. Large beads are formed of a size of 1-5 mm in diameter. The person of ordinary skill in the art, seeking to obtain microcapsules of a size very greatly smaller than the capsules made according to the Silbiger system, and noting the relative complexity of the Silbiger system, would never want to attempt to modify Sato to substitute Silbiger's complex and expensive system with Sato's simple system, with uncertain results at best.

The second point applicants wish to emphasis relates to what occurs after applicants' microcapsules are

initially formed. According to the present invention, and in order to increase the bioavailability of the encapsulated material, the calcium alginate shell, applicants' second coating, must then be weakened. This is accomplished by the acid rinse which dissolves away much of the calcium. Please see Dr. Blatt's Declaration in this regard.

The rejection relies upon Kantor as allegedly showing an acid rinse, but Kantor does **not** show any such acid rinse. Instead, Kantor uses an acid solution in the **formation** of microcapsules formed of a different material in a different way, not in any after-treatment carried out subsequent to the formation of microcapsules. The pertinent part of Kantor appears at column 2, commencing at line 23 as follows:

> The microcapsule [*sic*] are formulated from an emulsion of fish oil and enteric coating suspended in a basic solution, preferably a 25 % suspension of ethyl cellulose in ammonium hydroxide. The emulsion is atomized into an acidic solution using an inert gas….

One could say that Kantor discloses forming microcapsules by atomizing a basic emulsion into an acidic solution, but one cannot accurately say that Kantor teaches washing already formed microcapsules having a calcium alginate shell in an acidic solution.

Again, please see the attached Declaration of Dr. Blatt. Please note the test results shown such Declaration which shows that the acid wash removed calcium ion from the microcapsules. Such removal of calcium from the alginate shells in turn increases the bioavailability of the encapsulated material. This is all unobvious from Sato or Sato in view of any known prior art, including Silbiger and Kantor.

Withdrawal of the rejections is in order and is respectfully requested.

Claims 5, 7, 19 and 23-25 have been rejected under §103 as obvious over the same prior art as discussed above, further in view of Lim. This rejection is also respectfully again traversed.

Lim has not been cited to make up for the above-mentioned deficiencies of Sato or Sato in view of any of the other citations, and indeed does not do so. Claims 5, 7, 23 and 24 depend from and thus incorporate the subject matter of claim 1, and they are therefore patentable for the same reasons as pointed out above with respect to claim 1, even ignoring the dependent portions of these claims. Claim 19 depends from and incorporated the subject matter of claim 13, and thus is patentable for the same reasons as claim 13. Claim 25 is an independent claim which contains all the

features of claim 1, as well as additional detail, and claim 25 is patentable for the same reasons as pointed out above with respect to claim 1.

Withdrawal of the rejection is in order and is respectfully requested.

Applicants wish to respectfully re-emphasis a main point noted above, namely the unobviousness of the acid rinse. No prior art shows any such acid rinse or anything similar. Kantor, relied on for the use of an acidic solution, does not disclose any such or similar acid rinse as claimed. Therefore, even if the combination of Sato with Kantor were obvious (respectfully denied by applicants), applicants' process and resultant product could still not be achieved. The requirements for establishing a prima facie case of obviousness as set forth in MPEP 2143 simply do not exist.

Applicants believe that the issues raised in the Official Action have been fully addressed above in a manner warranting withdrawal of the prior art rejections and allowance of the claims. Such are respectfully requested. **However, if any problems remain, applicants respectfully request the examiner to telephone applicants' undersigned attorney at the number given below so that a personal**

interview can be scheduled prior to the issuance of any further Office Action.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By _____
Sheridan Neimark
Registration No. 20,520

SN:jaa
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\bn\m\makh\blatt2\pto\Amd 5may05 draft.doc